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STUDY OF RADIATION SICKNESS

- USSR -

Following is a translation of two articles in the Russian-language periodical Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (Pathological Physiology and Experimental Therapy), Vol VI, No. 5, Moscow, September-October, 1962. Complete bibliographic information accompanies each article.

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A COMPARISON OF THE CENTRAL DEPRESSING ACTION OF MEDINAL,
BARBAMIL, AND THIOPENTAL DURING ACUTE RADIATION
SICKNESS IN RATS AND RABBITS

- Czechoslovakia -

[Following is a translation of an article by M. Dostal, Gradets Kralove, Czechoslovakia, in the Russian-language periodical Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (Pathological Physiology and Experimental Therapy), Vol VI, No 5, Moscow, September-October 1962, pages 60-63.]

X-irradiation leads to injury of the liver. It may be suggested that the action of medicinal substances which are broken down by the liver is prolonged and reinforced after irradiation. We attempted to verify this proposition for barbiturates, since the interrelationship of their chemical structure and their metabolic fate are known.

The narcotic action of barbiturates (medinal, barbamil, thiopental) were compared in non-irradiated rats and in rats after total x-irradiation with a 600 r dose, and also in non-irradiated rabbits and rabbits irradiated with a 900 r dose; it was evaluated according to the extent of depression of unconditioned reflexes. The duration of the period during

which the animals remained in a forced position on their sides was the measure of this depression.

The rate of manifestation of the action of all the barbiturates tested in rats increased most on the 6th day after irradiation. The duration of the narcotic action of intravenously introduced barbamil was decreased on the 3rd day and increased on the 6th day after irradiation. On the 6th day after irradiation, fluctuation of the different values around the mean increased, in analysis by the F test, to such an extent that it assumed qualitative significance. The duration of the narcotic action of intraperitoneally introduced barbamil was also shortened on the 3rd day after irradiation. A narcotic dose of barbamil introduced intraperitoneally on the 6th day after irradiation was so toxic that 50% of the narcotized rats died. There thus appeared harder rats in which the extension of narcotic action and fluctuation of the different values around the mean was less than after intravenous introduction.

The duration of the narcotic action of intravenously and intraperitoneally introduced thiopental decreased on the 3rd day after irradiation. On the 6th day, the duration of the action of thiopental returned, after its intravenous introduction, to its initial value, and remained extended (unreliably) after intraperitoneal introduction. After both methods of introducing thiopental, fluctuations of the different values around the mean changed reliably. During the experiments, narcotic doses of barbiturates were introduced to the rabbits

repeatedly on the 3rd and 11th day after irradiation. The results of the experiments are given in Table 2.

The rate of onset of the action of medinal in irradiated rabbits was not changed in comparison with unirradiated rabbits.

The duration of the narcotic action, defined as lasting from the first lifting of the head to spontaneous assumption of a flat position, diminished unreliably after the second introduction and approached its initial value after the third. The narcotic action of barbamil on the 3rd day after irradiation lasted for a shorter period than after its first introduction in non-irradiated rabbits. After the repeated introduction of barbamil to non-irradiated rabbits, the duration of its narcotic action decreased. After repeated introduction of barbamil to irradiated rabbits, the duration of its action was unchanged. Differing from the irradiated rabbits, the controls became accustomed to barbamil. In comparison with the results of the first introduction, the duration of the action of barbamil after the second and third introduction was decreased in control rabbits, and increased in the experimental rabbits on the 11th day after irradiation. The duration of the narcotic action of repeatedly introduced thiopental in control and irradiated rabbits was somewhat increased, but no accustomization to thiopental was observed. Thiopental acted somewhat longer in irradiated rabbits.

In evaluating the results, we did not take into account possible changes in the distribution of barbiturates or the

sensitivity of the central nervous system.

The duration of the narcotic action of barbamil increased on the 6th day after irradiation, which was evidently connected with retarded breakdown of barbamil by the liver cells which were affected during irradiation. This is substantiated by the absence of accustomization to repeatedly introduced barbamil in irradiated rabbits. This factor is absent in cases of the use of medinal, inasmuch as it is completely eliminated by the kidneys in an unaltered form. These conclusions are inapplicable to experiments with thiopental, since thiopental enters into interaction with lipoids, which complicates the problem of the mechanism of its action.

TABLE 1. Rate of Onset and Duration of the Narcotic Action of Barbiturates in Rats Irradiated With 600 r.

	Method of introduction	Medinal						Barbital						Intrapanal					
		3-B			6-B			3-B			6-B			3-B			6-B		
		K	O		K	O		K	O		K	O		K	O		K	O	
Rate of onset of action	Intravenously	12.8 ± 2.2 (13)	9.3 ± 4.4 (9)	12.8 ± 2.2 (13)	8.9 ± 2.0 (20)														
	Intra-peritoneally	39.6 ± 9.7 (10)	36.4 ± 15.6 (7)	30.6 ± 0.7 (10)	28.3 ± 3.8 (11)	3.2 ± 0.6 (9)	4.0 ± 1.0 (9)	3.6 ± 0.6 (14)	2.1 ± 0.3 (14)	2.5 ± 0.7 (10)	2.5 ± 0.3 (9)	2.8 ± 0.5 (10)	1.8 ± 0.5 (6)						
Duration of action	Intravenously	384 ± 46 (12)	304 ± 49 (9)	381 ± 48 (12)	253 ± 54 (13)	25 ± 5 (17)	16 ± 3 (8)	25 ± 5 (17)	58 ± 35 (9)	100 ± 17 (10)	52 ± 32 (9)	100 ± 17 (10)	94 ± 64 (13)						
	Intra-peritoneally	302 ± 47 (10)	212 ± 68 (7)	302 ± 47 (10)	210 ± 50 (10)	288 ± 82 (9)	170 ± 33 (9)	316 ± 131 (14)	480 ± 10 (7)	245 ± 94 (9)	178 ± 59 (9)	232 ± 93 (10)	313 ± 370 (4)						

Legend:

K - non-irradiated control rabbits; O - experimental (irradiated) rabbits. Mean values in minutes and their average t-multiple errors for $p = 0.05$ are presented in the first line. The number of rabbits in each group is indicated in parentheses on the second line. The barbiturates were introduced in the following doses: Medinal - intravenously, 250 mg/kg, intraperitoneally, 200 mg/kg; barbamil - intravenously, 50 mg/kg, intraperitoneally, 30 mg/kg.

TABLE 2. Duration (in minutes) of the Narcotic Action of Barbiturates Introduced Repeatedly to Rabbits Irradiated With 900 r.

Action of barbiturates	Medlonal						Barbamil		
	Day after irradiation								
	3-R		6-R		11-R		3-R		6-R
	X	O	X	O	X	O	X	O	X
Rate of onset of action	28±3.4 (11)	29±5.4 (11)	33±6.2 (12)	32±6.2 (12)	31±6.8 (9)	35±7.1 (6)			
Lifting of head	105±55 (11)	152±52 (11)	85±26 (11)	90±29 (11)	149±73 (9)	142±189 (8)	241±65 (10)	115±18 (10)	187±37 (11)
Side position	265±51 (10)	292±65 (10)	226±58 (12)	253±83 (9)	278±73 (9)	290±101 (5)	337±71 (10)	241±60 (10)	221±47 (11)
Flat position							287±77 (10)	162±65 (10)	187±39 (11)

TABLE 2 (cont'd)

Barbamil				Thiopental			
Day after irradiation							
11-R		3-R		0-R		11-R	
O	K	O	K	O	K	O	K
115±18 (10)	153±23 (8)	248±80 (7)	19±5.8 (11)	24±5.8 (10)	10.2±5.8 (11)	31±11 (10)	27±7.3 (10)
150±25 (10)	198±49 (8)	311±63 (7)	27±5.5 (10)	35±7.5 (10)	29±5.3 (11)	37±13.2 (11)	32±6.4 (10)
156±20 (10)	175±77 (8)	289±54 (7)					42±20.9 (6)

Legend: X - control (non-irradiated) rabbits; O - experimental (irradiated) rabbits. Mean values in minutes and their average t-multiple errors for $P=0.05$ are presented in the first line. The number of rabbits in each group is given in parentheses in the second line. The barbiturates were introduced intravenously in the following doses: medlonal - 150 mg/kg; barbamil - 50 mg/kg; thiopental - 25 mg/kg.

THE EFFECT OF ACCELERATIONS CREATED AT THE MOMENT
OF IRRADIATION OF ANIMALS ON THE COURSE OF
ACUTE RADIATION SICKNESS

- USSR -

[Following is a translation of an article by K. V. Ivanov, M. V. Zhukov, and M. G. Molchanova in the Russian-language periodical Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (Pathological Physiology and Experimental Therapy), Vol VI, No 5, September-October, 1962, pages 74-75.]

The characteristics of the general reaction of an organism to the combined action of radial accelerations produced by rotating animals in a centrifuge and irradiation by penetrating radiations was investigated. We found no mention of similar work in the literature available. The experiments were performed on 44 male mice weighing 110-120 grams. The basic (experimental) group (19 rats) were irradiated during rotation in the centrifuge. The animals (7) of the first control group were only rotated in the centrifuge, and the second (18) were subjected to the action of radiation alone. Conditions of irradiation by an RUM-3 apparatus were: 180 kv, 20 ma, 0.5 mm Cu 1 mm Al, skin focal distance 60 cm, intensity of dose 38.3 r/min, irradiation (and revolution) time 26 minutes, dose 1000 r.

Leukocytosis (116-198% of the initial content of leukocytes) was observed within 5 minutes after action in all the rats rotated on the centrifuge; the number of blood leukocytes was decreased (to 81-29%) in the rats irradiated without rotation. The most pronounced leukocytosis (140-180%) was noted in rats subjected to combined action. Leukopenia in the irradiated animals of both groups was identical on subsequent days.

The drop in body weight at the onset of the climax of radiation sickness in the experimental rats averaged $16 \pm 0.86\%$, and in the controls, $21.4 \pm 1.12\%$. The average duration of life in rats subjected to irradiation alone was 8.7 ± 0.7 , and in groups subjected to combined action, 10 ± 0.6 days. In the first case, 5 of 18 rats died from the 3rd-6th days, 7, from the 7th-10th days, and 6, from the 11th-13th days. In the second group of 19 rats, 3, 6, and 10 animals died during the corresponding periods. Thus, acceleration produced at the moment of irradiation under the conditions of our experiments did not aggravate radiation sickness, and the experimental animals died no earlier than those irradiated without rotation. Although the difference in weight change, average duration of life, and in survivability of the irradiated rats of the control and experimental groups was not statistically verified, the similar direction of the shifts observed does not rule out the appearance of a tendency toward a less pronounced form of them following combined action.

The characteristics of early manifestations of general primary and leukocyte reaction, described above, in each group of animals can be explained by the dissimilar extent of disturbance in cortical-subcortical interrelationships [1-4]. These differences appeared on the 2nd day during determination of sound sensitivity. Epilepsy in response to the ringing of a bell, observed before irradiation in four rats of the second control group, was not noted in these animals after irradiation, whereas the number of rats with increased motor excitation was twice as great after combined action.

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